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Temporal, spatial, and cell type-specific control of Cre-mediated DNA recombination in transgenic mice.

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We have developed a universal system for temporal, spatial, and cell type-specific control of gene expression in mice that (1) integrates the advantages of tetracycline-controlled gene expression and Cre-recombinase-loxP site-mediated gene inactivation, and (2) simplifies schemes of animal crosses by combination of two control elements in a single transgene. Two transgenic strains were generated in which the cell type-specific control was provided by either the retinoblastoma gene promoter or the whey acidic protein promoter. Both promoters drive the expression of the reverse tetracycline-controlled transactivator (rtTA). Placed in cis configuration to the rtTA transcription unit, the rtTA-inducible promoter directs expression of Cre recombinase. In both strains crossed with cActXstopXLacZ reporter mice, which have a loxP-stop of transcription/translation-loxP-LacZ cassette driven by chicken beta-actin promoter, Cre-loxP-mediated DNA recombination leading to LacZ expression was accurately regulated in a temporal, spatial, and cell type-specific manner. This approach can be applied to establishment of analogous mouse strains with virtually any promoter as systems to control gene regulation in a variety of cell types.

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